Product ingredient source information may be entitled to confidential treatment

DP BARCODE: D368329; **FILE SYMBOL No.**: 35935-TT; **PRODUCT**: Fluroxypyr Technical (II)

FEE

Date: January 26, 2010

SUBJECT: Product Chemistry Review of Fluroxypyr Technical (II) TGAI / MUP

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DP BARCODE: D368329
DECISION No.: 418027
File Symbol No.: 35935-TT
PRODUCT: Fluroxypyr technical (II) TGAI / MUP
PCC: 128968
REGISTRANT: Nufarm Limited
USE: Herbicide
FOOD USE: Yes

INTRODUCTION:

The registrant Nufarm Limited has submitted a registration application for the new technical/mup product Fluroxypyr technical (II). The fluroxypyr technical (II) TGAI / MUP is produced by [redacted]. In support of the application, the registrant has submitted 830 series group A and group B data with MRID Nos. 478209-01 thru 478209-03, a CSF for basic formulation (dated 08-03-09) and the product label. The registrant has claimed that the proposed product is substantially similar to the registered product with Reg. No. 35935-53. TRB has been asked to evaluate the product chemistry data submitted and determine the similarity of the proposed product to the registered product.

SUMMARY OF FINDINGS:

1. The registrant has submitted a basic formulation CSF (dated 08-03-09) for fluroxypyr technical (II) TGAI /MUP. The average purity of the active ingredient in TGAI/MUP is 98.0%, as determined by the five batch analysis. The proposed certified limits for the AI and the impurities are based on the standard certified limits as set forth in 40CFR§158.350(b)(2). The product chemistry data submitted corresponding to guideline reference 830.1550 (product identity & composition) and 830.1750 (certified limits) satisfy the data requirements of 40CFR§158.320 and 158.350 respectively [MRID No. 478209-01].

2. The product chemistry data submitted corresponding to guideline reference 830.1600 (description of material used to produce the product) satisfy the data requirements of 40CFR§ 158.325 [MRID No. 478209-01].

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3. The product chemistry data submitted corresponding to guideline reference 830.1620 (description of production process) satisfy the data requirements for 40CFR§158.330. The manufacturing process for fluroxypyr technical (II) tgai / mup consists of [redacted]. The applicant has provided the details of the chemical process with reaction conditions, equipment used, working up procedures, and quality assurance steps [MRID No. 478209-01].

4. The product chemistry data submitted corresponding to guideline reference 830.1670 (discussion on the formation of impurities) satisfy the data requirements for 40CFR§158.340. During the production of fluroxypyr technical (II) tgai/mup, the registrant discussed the formation of [redacted] impurities present at the concentration of >0.1% including [redacted] No other impurities were reported during the 5 batch analysis. The registrant has stated that there is no possibility of the formation of impurities of toxicological concern as there are no preexisting conditions or starting materials present in the production process which are required for their formation [MRID No. 478209-01].

5. The data submitted corresponding the guideline reference 830.1700 (preliminary analysis) satisfy the data requirements of 40CFR§158.345. The study was conducted under GLP requirements in compliance with 40CFR§160 and OECD requirements. The analysis study was performed by Eurofins/Product Safety Laboratories, Dayton, NJ, USA. Five representative batches of the fluroxypyr technical (II) tgai/mup were analyzed for percent active ingredient and the impurities. The active ingredient and the organic impurities were identified and quantified by using HPLC-UV (225 nm) with external standard quantification method. [redacted]. The LOD's & LOQ's for all the impurities were determined. The analytical methods were validated for accuracy, linearity, and precision [MRID Nos. 478209-02].

6. The data submitted corresponding the guideline reference 830.1800 (enforcement analytical method) satisfy the data requirements of 40CFR§158.355. The purity of the AI in the TGAI was determined by HPLC-UV by external standard method. The analytical method utilized Agilent Zorbax SB-C18 column, 250 mm x 4.6 mm, 5 µm particle size, with UV detector operating at 225 nm. The method was validated for precision, accuracy and linearity [MRID Nos. 478209-01].

7. The data submitted or cited corresponding to 830 series group B (physical-chemical properties) satisfy the data requirements of 40CFR§158.310 (e). One year studies corresponding to guidelines storage stability (830.6317) and corrosion characteristics (830.6320) are in progress [MRID No. 478209-03].

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CONCLUSIONS:

The TRB has reviewed the product chemistry data submitted for fluroxypyr technical (II) TGAI/MUP (produced by [redacted]) and has concluded that:

1. All the product chemistry data submitted & cited corresponding to the guidelines 830 Series group A and group B are acceptable, except for storage stability (830.6317) and corrosion characteristics (830.6320).

2. The proposed CSF for basic formulation (dated 08-03-09) is acceptable.

3. The registrant must conduct the one year storage stability (830.6317) and corrosion characteristics (830.6320) studies for the proposed fluroxypyr technical (II) tgai/mup under full GLP requirements. It is recommended that the observations should be made at the intervals of 0 (initial), 3 month, 6 month, 9 month, and 12 month (final). The results must be submitted to the Agency on completion.

4. The proposed product (File Symbol No. 35935-TT) was determined to be substantially similar to the registered product with Reg. No. 35935-53 from the product chemistry point of view.

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830.1550. Product identity & Composition: (MRID No. 478209-01)

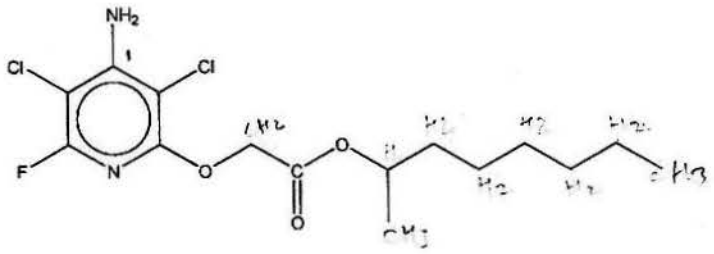
CAS No.:	81406-37-3
Common name/alias:	Fluroxypyr-meptyl
Chemical Names:	
IUPAC:	(*RS*)-1-methylheptyl 4-amino-3,5-dichloro-6-fluoro-2-pyridyloxyacetate
CAS:	1-methylheptyl [(4-amino-3,5-dichloro-6-fluoro-2-pyridinyl)oxy]acetate
Molecular formula:	$C_{15}H_{21}Cl_2FN_2O_3$
Molecular weight:	367.24
Structure:	

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Table 1. Manufacturing and Impurity Data for fluroxypyr technical II TGAI / MUP

GLN	Requirement	MRID	Status	Details and /or Deficiency
830.1550	Product Identity and composition	Basic CSF (08-03-09)	A	The NC of AI (98.0%) is supported by [redacted] batch analysis & agrees with the label claim nominal concentration. [redacted] impurities are listed on the CSF including [redacted]
8301600	Description of materials used to produce the product	478209-01	A	The description & composition for all the starting materials used to produce the fluroxypyr technical II (in [redacted]) have been provided by the registrant [redacted].
830.1620	Description of production process	478209-01	A	The production process has been described in full details.
830.1670	Discussion of formation of impurities	478209-01	A	The registrant has provided the complete mechanisms of formation, quantification and identification of all the impurities present in the product.
830.1700	Preliminary analysis	478209-02	A	[redacted] representative batches fluroxypyr technical II (produced in [redacted] were analyzed for percent active ingredient and the impurities. The HPLC-UV (225 nm) method was used for the identification of the AI and the impurities. The [redacted] batch analysis supported the proposed CSF for basic formulation. [redacted].
830.1750	Certified limits	478209-01	A	The proposed certified limits for the AI and impurities are based on standard certified limit table set-forth in 40CFR§158.350(b)(2).
830.1800	Enforcement analytical method	478209-01	A	The HPLC-UV (225 nm) with external standard method was used for the determination of the AI content in the TGAI/MUP. The method was validated for precision, linearity and accuracy.

A = Acceptable; N = unacceptable (see Deficiency); N/A = Not Applicable; G = Data gap; I = In progress or need upgrade; U = Up-grade (additional information required

830 Series group B (Physical-Chemical Properties)

Table 2: Physical and Chemical Properties of : Fluroxypyr technical II TGAI / MUP (China)

GLN	Requirement	MRID	Status	Result or Deficiency
830.6302	Color	cited 475407-03	A	Off white
830.6303	Physical state	" " "	A	Solid
830.6304	Odor	" " "	A	Faint odor
830.6313	Stability to normal and elevated temperatures, metals, and metal ions	" " "	A	Stable to Fe powder, iron acetate, Al powder and Al acetate at 54°C and at room temperature
830.6314	Oxidation/reduction: chemical incompatibility	478209-03	A	No reaction with water, Fe powder, Monoammonium phosphate, potassium permanganate & kerosene
830.6315	Flammability	Data matrix	W	Waiver request accepted
830.6316	Explodability	" " "	W	Waiver request accepted
830.6317	Storage stability	" " "	I	1 year study in progress
830.6319	Miscibility		NA	
830.6320	Corrosion characteristics	Data Matrix	I	1 year study in progress
830.7000	pH (cited)	475407-03	A	3.30 at 25°C
830.7050	UV/Visible absorption (cited)	" " "	A	Acid: λ = 210 nm; ε max = 41010.1 Base: λ = 219 nm; ε max = 23804.7 Neutral: λ = 210 nm; ε max = 40673.4
830.7100	Viscosity		NA	
830.7200	Melting point (cited)	475407-03	A	58.8°C
830.7220	Boiling point		NA	
830.7300	Density (cited)	475407-03	A	1.2455 g/ml @ 25°C
830.7370	Dissociation constants in water (DC) (cited)	" " "	A	No measurable DC could be determined in water
830.7550	Partition coefficient	478209-03	A	Log Po/w = 5.40
830.7840	Water solubility:	" " "	A	Water = 0.162 mg/l at 20°C; **See Note 1 for organic solvents**
830.7950	Vapor pressure (cited)*	" " "	A	1.349 x 10^{-3} mPa at 20°C

A = Acceptable; N = unacceptable (see Deficiency); N/A = Not Applicable; G = Data gap; I = In progress or need upgrade; U = Upgrade (additional information required); TBA = To Be Assigned

* The pesticide Manual 11th Edition, British Crop Protection Council.

Note1. 830.7840 (solubility) at 20°C: (MRID No. 478209-03)

Methanol = 607.25 g/L; Dichloromethane = 969.56 g/L; Hexane = 69.40 g/L.

830.1800. Enforcement of analytical method: (MRID No. 478209-01)

The five batches of the fluroxypyr technical II were assayed by a validated analytical method based on HPLC employing an external standard technique using UV detector.

Apparatus & parametrs

Instrument: Agilent 1100 HPLC
HPLC column: Agilent Zorbax SB-C18, 250 mm x 4.6 mm, 5 µm
Column temperature: 30°C
Flow rate: 1.0 ml/min
Injection volume: 10 µl
UV detector wavelength: 225 nm
Retention time for Fluroxypyr-meptyl: approximately 17.9 minutes.
Mobile phase: A = water + trifluoroacetic acid adjusted to pH 3
B = acetonitrile

Time (min)	% A	% B
0	50	50
2	50	50
15	10	90
17	10	90
19	50	50
25	50	50

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CONFIDENTIAL APPENDIX

Proposed basic CSF (dated 08-03-09)

[redacted]

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